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Risk Factors Associated with Miscarriage and Impaired Fecundity among United States Servicewomen during the Recent Conflicts in Iraq and Afghanistan

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A B S T R A C T

Background: Research on the reproductive health of U.S. servicewomen deployed in support of the recent operations in Iraq and Afghanistan is sparse. The objective of this study was to evaluate whether military experiences, including combat deployment, deployment length, and life stressors during the recent conflicts, were associated with increased odds for miscarriage or impaired fecundity among U.S. servicewomen.

Methods: We used data from the Millennium Cohort Study, a large longitudinal military study that began in 2001 and includes military personnel from all service branches, including active duty and Reserve/National Guard personnel. Participants for this study included women aged 18 to 45 years who had completed two questionnaires (2004–2006 and 2007–2008). Separate multivariable logistic regression models were performed to estimate the odds of reporting miscarriage and impaired fecundity by military experiences that adjusted for covariates. Subanalyses were conducted using *International Classification of Diseases, Ninth Revision, Clinical Modification* codes found in the Military Health System Data Repository for both outcomes among servicewomen on active duty.

Results: Overall, 31% and 11% of military servicewomen reported miscarriage and impaired fecundity, respectively, during the approximate 3-year follow-up period. After adjusting for demographic, behavioral, and military characteristics, deployment experiences and life stressors were not associated with miscarriage or perceived impaired fecundity. Subanalyses using medical record data confirmed these results.

Conclusions: Overall, these results suggest that military deployments do not increase risk for miscarriage and impaired fecundity among U.S. servicewomen. However, because the point estimates for many of the exposures were elevated, more research is needed to better understand the potential risks associated with environmental exposures and specific types of combat exposures.

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Women account for 14.6% of the U.S. Armed Forces, with more than 200,000 women deploying in support of the recent conflicts in Iraq and Afghanistan ("Women in Military Service for America Memorial Foundation Inc.," 2010). Before these conflicts, the number of women who deployed was much smaller, and women servicemembers often served in noncombat roles ("Iraq and Afghanistan Veterans of America," 2009). However, during the recent conflicts, servicewomen have reported in-theater combat experiences. This is in part due to the absence of traditional battle lines (Vogt et al., 2011) as well as recent policy changes allowing women to take on a wider range of duties, including infantry roles on combat teams, thereby increasing their exposures to combat and intense stress (Joint Chiefs of Staff, 2013). With an increasing number of servicewomen deploying and experiencing combat, there is a growing need to evaluate if these experiences adversely affect reproductive health ("Iraq and Afghanistan Veterans of America," 2009).

Deployments to the recent conflicts in Iraq and Afghanistan may have exposed women to both military-unique experiences as well as traditional factors associated with miscarriage and/or infertility. One known factor that has been associated with miscarriage and infertility is stress. The exact biological mechanism for which stress is believed to cause these adverse outcomes has not been confirmed, but the literature suggests that the immune and hormone alterations caused by stress may lead to reproductive failure (Agarwal, Aponte-Mellado, Premkumar, Shaman, & Gupta, 2012; Madhappan et al., 2003; Nakamura, Sheps, & Arck, 2008). Given that research in nonmilitary populations indicates that experiencing life stressors has an adverse effect on reproductive outcomes, it is important to determine if the unique stressors of military deployments are associated with adverse reproductive outcomes, such as miscarriage and impaired fecundity.

Previous research investigating the association of deployment with miscarriage and impaired fecundity among U.S. servicewomen is sparse and most of this research has focused on veterans (Araneta et al., 2004; Armed Forces Health Surveillance Center, 2012; Doyle et al., 2004; Doyle, Maconochie, & Ryan, 2006; Kang et al., 2001; Katon et al., 2014; Mattocks et al., 2015; Wells et al., 2006). The majority of the miscarriage studies did not find an association of deployment to the 1991 Gulf War with miscarriage in pregnancies conceived after the war by women veterans (Doyle et al., 2004; Doyle et al., 2006; Kang et al., 2001; Wells et al., 2006). Although infertility among servicemembers and veterans who deployed in support of the operations in Iraq and Afghanistan has been studied, to our knowledge, only one previous report examined infertility among the current era of U.S. servicewomen (Armed Forces Health Surveillance Center, 2012). Two of the previous studies described the prevalence of infertility (~2% have received a diagnosis of infertility, 16% reported history of infertility) among women veterans who received care at a VA facility, although neither study reported the effects of specific deployment related-stressor (Katon et al., 2014; Mattocks et al., 2015). One previous report found longer duration of deployment associated with an increased risk for infertility (Armed Forces Health Surveillance Center, 2012). Moreover, the majority of these previous studies were limited by being cross-sectional or data linkage studies.

Exploring the relationship of recent deployments and combat-related experiences with miscarriage and impaired fecundity may help to better understand whether serving in the military has a negative effect on women's reproductive health. Our longitudinal study aimed to evaluate if U.S. military servicewomen who deployed and experienced combat during the recent conflicts in Iraq and Afghanistan subsequently experienced an increased odds of miscarriage or impaired fecundity. The Millennium Cohort Study, as the largest longitudinal military study in U.S. history, has the unique ability to prospectively investigate women's reproductive health in relation to military experiences.

Material and Methods

Study Population and Data Sources

The study population was derived from the Millennium Cohort Study, a longitudinal study designed to evaluate the impact of military service on the long-term health of U.S. servicemembers. Using an in-depth questionnaire, military, health, occupational factors, and life experiences were assessed prospectively at 3-year intervals. The methodology of the Millennium Cohort Study has been described previously (Ryan et al., 2007; Smith & Millennium Cohort Study, 2009). The study currently includes more than 200,000 participants who enrolled during four separate cycles between 2001 and 2013.

The population for the current study consisted of women from the first two enrollment cycles, or panels, who completed surveys during the 2004 through 2006 and 2007 through 2008 survey cycles. To be eligible, women had to be aged 18 to 45 years and to not have separated from the military before September 2001 ($n = 14{,}480$). After exclusion criteria, 3,366 women were included in the miscarriage analysis and 11,183 were included in the impaired fecundity analysis (Figure 1). The population for each outcome was stratified by panel owing to differing enrollment criteria. Exposures and covariates were measured on the 2004 through 2006 questionnaire, while outcomes were measured on the 2007 through 2008 questionnaire; therefore, for these analyses, the data collected from 2004 through 2006 are called baseline and the data collected from 2007 through 2008 are called follow-up (Figure 2).

Data sources included the Millennium Cohort Study questionnaire and electronic Department of Defense (DoD) personnel data provided by the Defense Manpower Data Center. The Millennium Cohort Study questionnaire was used to assess self-reported data, including information on self-reported miscarriage, self-perceived impaired fecundity, combat exposures, and other lifestyle and health metrics. Electronic personnel data from Defense Manpower Data Center was used to assess deployments in support of the recent operations in Iraq and Afghanistan, and military and demographic characteristics. The study was approved by the institutional review boards Naval Health Research Center and San Diego State University, and informed consent was obtained from all participants.

Outcomes

We assessed two outcomes using data from the Millennium Cohort Study questionnaire: self-reported miscarriage and self-perceived impaired fecundity. Miscarriage was assessed using the question, "Have you had a miscarriage within the last 3 years?" to which participants could respond, "Yes," "No," or "Does Not Apply," on the follow-up questionnaire. Miscarriage was assessed among women who reported a pregnancy during the study time and had responded "Yes" or "No" to the miscarriage question.

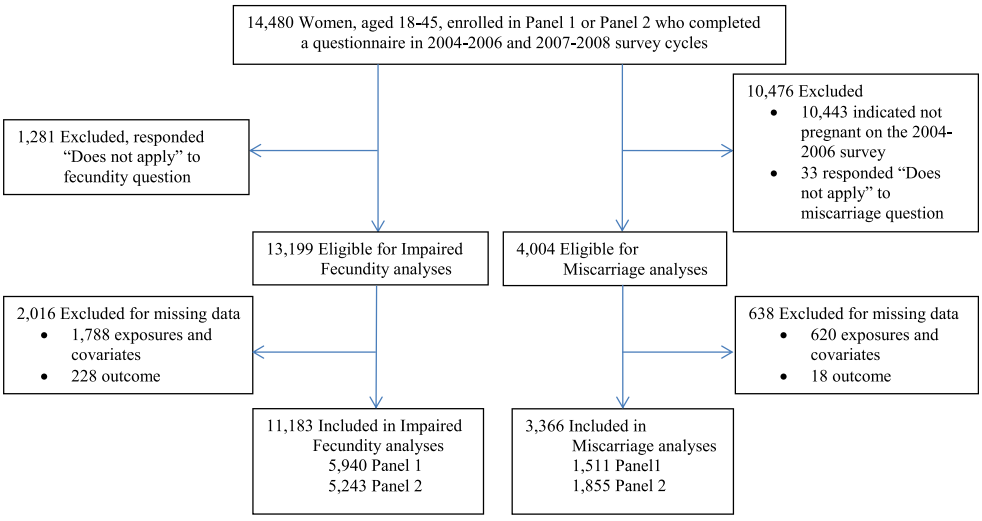

Figure 1. Study population.

Self-perceived impaired fecundity was assessed using the question on the follow-up questionnaire, "During the last 3 years have you tried and been unable to become pregnant?", with the same response options as the miscarriage question. Self-perceived impaired fecundity was assessed among women who responded "Yes" or "No" to the self-perceived impaired fecundity question.

In a subanalysis, medical encounter data obtained from the Military Health System Data Repository and methodology used by the DoD Birth and Infant Health Registry was used to assess the outcomes (Ryan et al., 2001). Miscarriage was determined by having at least one of the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnostic codes that indicate a pregnancy loss (ectopic/molar pregnancy: 630.xx–633.xx; other pregnancy with abortive outcome: 634.xx–639.xx; intrauterine death: 656.4x; outcome of delivery: V27.[1,3,4,6,7]), procedure (removal of ectopic/molar pregnancy: 66.62, 68.0, 74.3), or Current Procedural Terminology codes (treatment of molar/ectopic pregnancy: 59100, 59120, 59121, 59130, 59135, 59136, 59140, 59150, 59151, 59870) between 2004 and 2007. Pregnancies ending in elective abortions and those thought to have a miscoded pregnancy loss (owing to a live birth outcome up to 36 weeks after the suspected false code) were excluded from analyses. To assess infertility in the medical encounter data, the ICD-9-CM diagnostic codes used were 628.x (infertility diagnosis from a medical professional) (Conlin, Bukowinski, Sevick, DeScisciolo, & Crum-Cianflone, 2013).

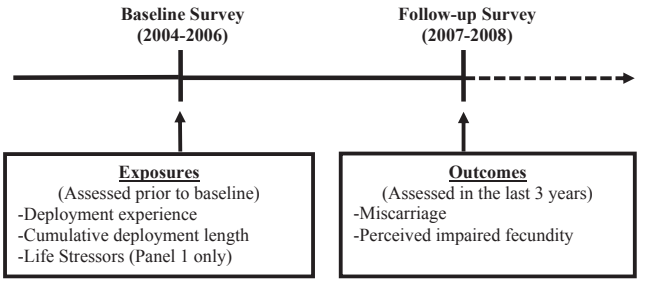

Figure 2. Study design.

Main Exposures of Interest

The three main exposures assessed in these analyses were deployment status, cumulative days deployed, and life stressors. The two deployment-related exposures were determined using electronic DoD personnel files that include deployment dates for those deployed since September 11, 2001. Participants who returned from deployment before completing their baseline questionnaire were considered deployed. Deployment status was categorized as nondeployed, deployed without combat, and deployed with combat. Among those deployed, combat experience was determined based on at least one positive response of being personally exposed to dead and/or decomposing bodies, maimed soldiers or civilians, prisoners of war/refugees, witnessing death, or witnessing physical abuse (torture, beating, rape). Cumulative deployment length was calculated as the total number of days deployed within the 3-year period before their baseline questionnaire submission and was categorized as 0, 1 to 180, and more than 180 days. The third exposure, life stressors, was assessed at baseline among panel 1 participants only using questions on the Millennium Cohort questionnaire. Panel 1 participants indicated if they had experienced any of the listed stressors in the past 3 years, such as divorce or separation, major financial problems, and forced sexual relations or sexual assault. Participants were classified as having low/mild or moderate/major life stressors based on a modified version of the Social Readjustment Rating Scale scoring system (Hobson et al., 1998; Holmes, 1982). Life stressors were not examined among the panel 2 participants because these items were assessed as lifetime stressors.

Covariates

Covariates were selected based on previous research indicating an association with reproductive health outcomes or because they were of interest to the military. Demographic characteristics were assessed using electronic personnel files and included sex, birth date, highest education level, marital status, race/ethnicity, pay grade, service component, service branch, and occupation at baseline.

Several characteristics were assessed using self-reported data from the baseline questionnaire. These characteristics are modifiable behaviors that are known to have negative reproductive health effects. Current, past, and nonsmokers were identified based on self-report of having smoked at least 100 cigarettes (five packs) in their lifetime and if they had successfully quit smoking (Smith et al., 2008). Heavy weekly drinking was defined as consuming more than seven drinks per week (Jacobson et al., 2008). Alcohol-related problems were assessed using the Patient Health Questionnaire alcohol screening tool; participants who reported at least one risky drinking behavior, such as driving under the influence more than once over the past 12 months, screened positive for alcohol-related problems (Jacobson et al., 2008; Spitzer, Williams, Kroenke, Hornyak, & McMurray, 2000; Spitzer et al., 1994).

Posttraumatic stress disorder (PTSD) was assessed using data from the PTSD Checklist-Civilian Version. A positive PTSD screen was based on criteria established in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (Brewin, 2005; Spitzer, Kroenke & Williams, 1999). Using a standardized Patient Health Questionnaire scoring mechanism, major depression, panic syndrome, and other anxiety syndrome were assessed (Kroenke, Spitzer, & Williams, 2001; Spitzer et al., 1999; Spitzer et al., 2000; Spitzer et al. 1994). Participants were classified as having a positive psychiatric history if they screened positive for one or more of the following: PTSD, major depression, panic syndrome, or other anxiety syndrome. Psychotropic medication use was assessed based on self-report of medication for anxiety, depression, or stress on the baseline questionnaire.

Prior medical conditions that may be associated with adverse reproductive outcomes were assessed based on self-report of provider-diagnosed conditions and included hypertension, thyroid condition other than cancer, seizures, lupus, diabetes or sugar diabetes, rheumatoid arthritis, or frequent bladder infections. Participants were classified as having none of these conditions or one or more condition(s). Data on body mass index were analyzed by using self-reported weight and height and categorized as underweight/normal ($\leq$24.9 kg/m^2), overweight (25–29.9 kg/m^2), or obese ($\geq$30 kg/m^2).

Exposures to pesticides and chemicals were assessed based on self-report of being personally exposed to pesticides (including creams, sprays, or uniform treatments) or with pesticides applied in the environment or around living spaces; occupational hazards requiring protective equipment, such as respirators or hearing protection; or routine skin contact with paint and/or solvents and/or substances. The number of pesticide and chemical exposures reported was summed and categorized as zero, one, or two.

Statistical Methods

Univariate analyses were used to assess the relationship between the two outcomes of miscarriage and self-perceived impaired fecundity, the three main exposures, and all covariates. Separate analyses were performed for each panel. Multivariable logistic regression models were performed using separate models for each outcome (miscarriage and self-perceived impaired fecundity) and each of the three main exposures (deployment status, cumulative days deployed, and life stressors). Each model was adjusted for covariates that were found to be significant ($p < .05$), confounders (>10% change in the exposure estimate), and covariates that are of interest regardless of significance (a priori defined as age, occupation, and pesticide and chemical exposures). The Hosmer–Lemeshow test was used to test model fit and multicollinearity was assessed using a variance inflation factor of four or higher.

Subanalyses were conducted using objective medical encounter data obtained from the Military Health System Data Repository to define both miscarriage and infertility using a subset of active duty study participants. Survival analysis using Cox proportional hazard models was performed because these data included date of diagnosis. Participants were censored at the diagnosis date, date of separation from military service, or follow-up survey date, whichever occurred first. All analyses were completed using SAS statistical software, version 9.3 (SAS Institute, Inc., Cary, NC).

Results

Miscarriage

A total of 1,045 of 3,366 servicewomen (31.0%) between the ages of 18 and 45 years who had a pregnancy reported a miscarriage during the approximate 3-year follow-up period. Notably, women in panel 1 who reported a miscarriage were proportionally more likely to be older, college educated, and officers; in addition, they were more likely to report one or more prior medical conditions, prior miscarriage, and previous impaired fecundity (Table 1). Women in panel 2 who reported a miscarriage were proportionally more likely to be past smokers; they were also more likely to report psychiatric symptoms, prior miscarriage, and impaired fecundity.

In the adjusted model, deployment experiences, with or without combat, were not associated with reporting miscarriage in either panel 1 or 2 (Table 2). In separate models, cumulative days deployed was not associated with reporting miscarriage in either panel 1 or 2 and reporting life stressors was not associated with reporting miscarriage in panel 1 (Table 2). Subanalyses completed using medical record data showed 136 miscarriage events among 1,041 eligible women. Consistent with the self-report findings, no associations were found between any of our main exposures and miscarriage in the multivariable models (data not shown).

Factors associated with miscarriage in panel 1 included age (for every 5-year incremental increase in age, adjusted odds ratio [AOR], 1.49; 95% confidence interval [CI], 1.31–1.70), marital status (married women: AOR, 0.76; 95% CI, 0.60–0.98), prior medical condition (AOR, 1.44; 95% CI, 1.05–1.97), and prior history of a miscarriage (AOR, 3.95; 95% CI, 2.96–5.26). Among women in panel 2, factors associated with higher odds of miscarriage included smoking (past smokers, AOR, 1.34; 95% CI, 1.02–1.76) and prior history of miscarriage (AOR, 3.83; 95% CI, 2.93–5.00; data not shown in tables).

To account for the possibility that some factors may mediate or confound the relationship between the main exposures and miscarriage, we reran the models without prior medical conditions and smoking status. Findings were consistent with the final models for both the combat exposure and cumulative days deployed, where miscarriage was not found to be associated with these exposures. However, life stressors were found to be marginally significant when these variables were removed from the panel 1 model (AOR, 1.75; 95% CI, 1.04–2.94; data not shown).

Table 1
Demographic, Military, Behavioral, and Health Characteristics of Millennium Cohort Servicewomen by Self-Reported Miscarriage* Status

Characteristics†	Panel 1 (n = 1,511)		Panel 2 (n = 1,855)	
	No Miscarriage (n = 1,038)	Miscarriage (n = 473)	No Miscarriage (n = 1,283)	Miscarriage (n = 572)
Mean ± SD age	32.8 ± 4.6	34.4 ± 5.4	27.1 ± 3.8	27.4 ± 4.5
Education				
Some college or less	673 (64.8)	280 (59.2)	1,072 (83.6)	489 (85.5)
Bachelor's degree or higher	365 (35.2)	193 (40.8)	211 (16.4)	83 (14.5)
Marital status				
Not married	336 (32.4)	162 (34.3)	827 (64.5)	380 (66.4)
Married	702 (67.6)	311 (65.8)	456 (35.5)	192 (33.6)
Race/ethnicity				
Non-Hispanic White	667 (64.3)	296 (62.6)	852 (66.4)	374 (65.4)
Non-Hispanic Black	166 (16.0)	84 (17.8)	203 (15.8)	91 (15.9)
Other	205 (19.7)	93 (19.7)	228 (17.8)	107 (18.7)
Service component				
Reserve/National Guard	621 (59.8)	291 (61.5)	452 (35.2)	199 (34.8)
Active duty	417 (40.2)	182 (38.5)	831 (64.8)	373 (65.2)
Service branch				
Army	549 (52.9)	243 (51.4)	609 (47.5)	290 (50.7)
Navy/Coast Guard	183 (17.6)	80 (16.9)	244 (19.0)	113 (19.8)
Marine Corps	23 (2.2)	11 (2.3)	42 (3.3)	10 (1.7)
Air Force	283 (27.3)	139 (29.4)	388 (30.2)	159 (27.8)
Occupation				
Administration and supply	451 (43.4)	200 (42.3)	502 (39.1)	228 (39.9)
Combat specialist	73 (7.0)	31 (6.6)	78 (6.1)	48 (8.4)
Health care	218 (21.0)	118 (24.9)	229 (17.8)	103 (18.0)
Other	296 (28.5)	124 (26.2)	474 (36.9)	193 (33.7)
Pay grade				
Enlisted	770 (74.2)	315 (66.6)	1,131 (88.2)	508 (88.8)
Officer	268 (25.8)	158 (33.4)	152 (11.8)	64 (11.2)
Pesticide/chemical exposures‡				
None	528 (50.9)	230 (48.6)	557 (43.4)	225 (39.3)
1	280 (27.0)	126 (26.6)	385 (30.0)	188 (32.9)
2	230 (22.2)	117 (24.7)	341 (26.6)	159 (27.8)
Body mass index				
Underweight/normal	562 (54.1)	266 (56.2)	838 (65.3)	363 (63.5)
Overweight	355 (34.2)	151 (31.9)	360 (28.1)	180 (31.5)
Obese	121 (11.7)	56 (11.8)	85 (6.6)	29 (5.1)
Psychotropic medication use§				
No	974 (93.8)	433 (91.5)	1,212 (94.5)	534 (93.4)
Yes	64 (6.2)	40 (8.5)	71 (5.5)	38 (6.6)
Psychiatric symptoms‖				
No	951 (91.6)	419 (88.6)	1,148 (89.5)	488 (85.3)
Yes	87 (8.4)	54 (11.4)	135 (10.5)	84 (14.7)
Prior medical history¶				
None	904 (87.1)	379 (80.1)	1,130 (88.1)	494 (86.4)
1 or more condition(s)	134 (12.9)	94 (19.9)	153 (11.9)	78 (13.6)
Smoking status				
Never smoker	681 (65.6)	316 (66.8)	784 (61.1)	336 (58.7)
Past smoker	113 (10.9)	60 (12.7)	211 (16.4)	126 (22.0)
Current smoker	244 (23.5)	97 (20.5)	288 (22.4)	110 (19.2)
Heavy weekly drinking#				
No	954 (91.9)	433 (91.5)	1,162 (90.6)	509 (89.0)
Yes	84 (8.1)	40 (8.5)	121 (9.4)	63 (11.0)
Alcohol-related problems**				
No	986 (95.0)	449 (94.9)	1,165 (90.8)	511 (89.3)
Yes	52 (5.0)	24 (5.1)	118 (9.2)	61 (10.7)
Previously reported miscarriage††				
No	932 (89.8)	320 (67.7)	1,168 (91.0)	410 (71.7)
Yes	106 (10.2)	153 (32.3)	115 (9.0)	162 (28.3)
Previously reported impaired fecundity‡‡				
No	903 (87.0)	386 (81.6)	1,142 (89.0)	482 (84.3)
Yes	133 (12.8)	86 (18.2)	141 (11.0)	89 (15.6)

* Self-report of miscarriage on the follow-up survey.
† All characteristics assessed from the baseline survey, except for age, which was assessed using the follow-up survey.
‡ Variable measures exposure to pesticides and chemical exposures. The variable was based on self-report of exposure to occupational hazards requiring protective equipment, routine skin contact with paint and/or solvent and/or substances, pesticides applied to the environment, living spaces, and/or to yourself and/or clothing.
§ Self-reported use of medication to treat anxiety, depression, or stress.
‖ Assessed using screening tools for posttraumatic stress disorder, depression, anxiety, or panic.
¶ Self-report of physician diagnosis to any of the following: hypertension, thyroid condition other that cancer, seizures, lupus, diabetes or sugar diabetes, rheumatoid arthritis, and/or frequent bladder infections.
# Heavy weekly drinking is defined as consuming more than seven drinks per week.
** Alcohol-related problems was assessed using the Patient Health Questionnaire.
†† Self-reported miscarriage at baseline.
‡‡ Self-reported infertility at baseline is not included in main analyses for the miscarriage population. Frequencies are given as a part of subanalyses. Number of people missing this variable in Panel 1 = 3, Panel 2 = 1.

Table 2
Frequencies, Prevalence, and AOR of Miscarriage* among Servicewomen in the Millennium Cohort

Models	Panel 1† (*n* = 1,511)			Panel 2‡ (*n* = 1,855)		
	n (%)*	AOR	95% CI	*n* (%)*	AOR	95% CI
Deployment status§						
Nondeployed	357 (30.9)	1.00		416 (30.7)	1.00	
Deployed, without combat	53 (27.8)	1.05	(0.73–1.51)	54 (26.1)	0.86	(0.61–1.22)
Deployed, with combat	63 (38.7)	1.41	(0.96–2.07)	102 (34.7)	1.16	(0.87–1.56)
Cumulative days deployed‖						
0	357 (30.9)	1.00		416 (30.7)	1.00	
1–180	55 (32.0)	1.22	(0.84–1.77)	68 (30.0)	1.01	(0.73–1.39)
>180	61 (33.5)	1.18	(0.82–1.71)	88 (32.1)	1.05	(0.77–1.42)
Life stressors¶						
Low/mild	441 (30.6)	1.00				
Moderate/major	32 (45.1)	1.67	(0.99–2.80)			

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.

* Number and 3-year cumulative prevalence of self-reported miscarriage at follow-up.

† Models are adjusted for age, marital status, occupation, pesticide and chemical exposures, adverse prior medical history, and prior miscarriage at baseline.

‡ Models adjusted for age, occupation, pesticide and chemical exposures, smoking status, and prior miscarriage at baseline.

§ Combat was defined as self-report of having personally experienced at least one of the following combat or combat-like situations: witnessing a person's death due to war, disaster, or tragic event; witnessing instances of physical abuse (torture, beating, rape); dead and/or decomposing bodies; maimed soldiers or civilians; and prisoners of war or refugees. This was assessed on the baseline survey as having occurred during the past 3 years.

‖ Cumulative length deployed was assessed as the total number of days deployed from 3 years before the baseline assessment to the day the baseline survey was completed.

¶ Life stressors was assessed using scoring mechanisms adapted from the Holmes and Rahe Social Readjustment Rating Scale.

Self-Perceived Impaired Fecundity

A total of 1,268 of 11,183 women (11.3%) between the ages of 18 and 45 years self-reported impaired fecundity. Notably, women in panel 1 who reported self-perceived impaired fecundity were proportionally more likely to be married and report a prior miscarriage or previous impaired fecundity (Table 3). Women in panel 2 who reported self-perceived impaired fecundity were proportionally more likely to be married, active duty servicemembers, and past smokers; in addition, they were more likely to report psychiatric symptoms, one or more prior medical conditions, prior miscarriage, and previous impaired fecundity.

In the adjusted models, deployment experiences, with or without combat, were not associated with reporting self-perceived impaired fecundity in panel 1 or 2 (Table 4). In separate models, cumulative days deployed was not associated with reporting self-perceived impaired fecundity in either panel 1 or 2, nor was life stressors in panel 1 (Table 2). Subanalyses using medical record data found 213 events of infertility in 4,079 eligible women. Consistent with the self-reported findings, no associations were found between any of the main exposures and infertility in multivariable models (data not shown).

Among women in panel 1, factors associated with higher odds of perceived impaired fecundity included race/ethnicity (non-Hispanic Black women in comparison with non-Hispanic White women: AOR, 1.34 [95% CI, 1.07–1.68]; other race/ethnicity: AOR, 1.27 [95% CI, 1.01–1.61]), heavy weekly drinking (AOR, 1.40; 95% CI, 1.07–1.84), and previous impaired fecundity (AOR, 14.45; 95% CI, 11.78–17.74). Among the women in panel 2, factors associated with higher odds of perceived impaired fecundity included race/ethnicity (non-Hispanic Black women, in comparison to non-Hispanic White women: AOR, 1.34; 95% CI, 1.04–1.72), age (for every 5-year incremental increase in age: AOR, 1.16; 95% CI, 1.01–1.33), psychiatric symptoms (AOR, 1.48; 95% CI, 1.15–1.90), smoking (past smokers, AOR, 1.52; 95% CI, 1.21–1.92), and previously reported self-perceived impaired fecundity (AOR, 6.91; 95% CI, 5.55–8.61; data not shown in tables).

To account for the possibility that some factors may mediate or confound the relationship between perceived impaired fecundity, we reran the models without heavy weekly drinking, psychiatric symptoms, and smoking status. Findings were consistent with the final models for the combat exposure, cumulative days deployed, and life stressors, where perceived impaired fecundity was not found to be associated with these exposures (data not shown).

Discussion

Our findings suggest experiencing deployment and combat-related exposures are not associated with miscarriage and self-perceived impaired fecundity among a large cohort of military women who served during the recent conflicts. Moreover, self-reported findings in all models were consistent with objective outcome data when assessed using medical records. Although none of the main exposures were found to be statistically significant in association with miscarriage or impaired fecundity, the point estimate for those deployed with combat experience were increased for all models. Overall, these findings indicate that recent deployment and combat experiences do not seem to have significant adverse effects at a population level on servicewomen's reproductive health. However, because the point estimates for many of the exposures were increased, more research is needed to understand potential risks associated with specific exposures, such as combat. Our findings indicate that life stressors, which have historically been associated negatively with reproductive health outcomes, and military-specific characteristics (such as service branch or component, occupation, and rank) were not associated with miscarriage or impaired fecundity after adjusting for additional factors.

Previous studies from the first Gulf War have found minimal associations between serving in combat-related roles and negative reproductive health conditions among men (Araneta et al., 2004; Doyle et al., 2004; Doyle et al., 2006; Kang et al., 2001; Wells et al., 2006). With the exception of one study

Table 3
Demographic, Military, Behavioral, and Health Characteristics of Millennium Cohort Servicewomen by Self-Perceived Impaired Fecundity*

Characteristics†	Panel 1 (n = 5,940)		Panel 2 (n = 5,243)	
	No Impaired Fecundity (n = 5,284)	Impaired Fecundity (n = 656)	No Impaired Fecundity (n = 4,631)	Impaired Fecundity (n = 612)
Mean ± SD age	35.7 ± 5.7	35.4 ± 5.4	27.9 ± 4.7	28.4 ± 5.0
Education				
Some college or less	3,398 (64.3)	414 (63.1)	3,656 (78.9)	506 (82.7)
Bachelor's degree or higher	1,886 (35.7)	242 (36.9)	975 (21.1)	106 (17.3)
Marital status				
Not married	2,378 (45.0)	255 (38.9)	3,391 (73.2)	405 (66.2)
Married	2,906 (55.0)	401 (61.1)	1,240 (26.8)	207 (33.8)
Race/ethnicity				
Non-Hispanic White	3,388 (64.1)	372 (56.7)	3,100 (66.9)	381 (62.3)
Non-Hispanic Black	985 (18.6)	155 (23.6)	696 (15.0)	115 (18.8)
Other	911 (17.2)	129 (19.7)	835 (18.0)	116 (19.0)
Service component				
Reserve/National Guard	3,080 (58.3)	357 (54.4)	2,113 (45.6)	248 (40.5)
Active duty	2,204 (41.7)	299 (45.6)	2,518 (54.4)	364 (59.5)
Service branch				
Army	2,662 (50.4)	335 (51.1)	2,203 (47.6)	306 (50.0)
Navy/Coast Guard	914 (17.3)	124 (18.9)	861 (18.6)	117 (19.1)
Marine Corps	126 (2.4)	17 (2.6)	119 (2.6)	13 (2.1)
Air Force	1,582 (29.9)	180 (27.4)	1,448 (31.3)	176 (28.8)
Occupation				
Administration and supply	2,391 (45.2)	294 (44.8)	1,687 (36.4)	222 (36.3)
Combat specialist	336 (6.4)	36 (5.5)	304 (6.6)	31 (5.1)
Health care	1,105 (20.9)	149 (22.7)	889 (19.2)	125 (20.4)
Other	1,452 (27.5)	177 (27.0)	1,751 (37.8)	234 (38.2)
Pay grade				
Enlisted	3,901 (73.8)	485 (73.9)	3,905 (84.3)	538 (87.9)
Officer	1,383 (26.2)	171 (26.1)	726 (15.7)	74 (12.1)
Pesticide/chemical exposures‡				
None	2,676 (50.6)	306 (46.6)	1,929 (41.7)	228 (37.3)
1	1,426 (27.0)	198 (30.2)	1,458 (31.5)	199 (32.5)
2	1,182 (22.4)	152 (23.2)	1,244 (26.9)	185 (30.2)
Body mass index				
Underweight/normal	2,893 (54.8)	359 (54.7)	3,143 (67.9)	382 (62.4)
Overweight	1,863 (35.3)	215 (32.8)	1,279 (27.6)	190 (31.0)
Obese	528 (10.0)	82 (12.5)	209 (4.5)	40 (6.5)
Psychotropic medication use§				
No	4,836 (91.5)	604 (92.1)	4,361 (94.2)	557 (91.0)
Yes	448 (8.5)	52 (7.9)	270 (5.8)	55 (9.0)
Psychiatric symptoms‖				
No	4,832 (91.4)	587 (89.5)	4,174 (90.1)	503 (82.2)
Yes	452 (8.6)	69 (10.5)	457 (9.9)	109 (17.8)
Prior medical history¶				
None	4,457 (84.3)	537 (81.9)	4,177 (90.2)	526 (85.9)
1 or more condition(s)	827 (15.7)	119 (18.1)	454 (9.8)	86 (14.1)
Smoking status				
Never smoker	3,446 (65.2)	419 (63.9)	3,017 (65.1)	347 (56.7)
Past smoker	686 (13.0)	95 (14.5)	732 (15.8)	143 (23.4)
Current smoker	1,152 (21.8)	142 (21.6)	882 (19.0)	122 (19.9)
Heavy weekly drinking#				
No	4,742 (89.7)	570 (86.9)	4,037 (87.2)	530 (86.6)
Yes	542 (10.3)	86 (13.1)	594 (12.8)	82 (13.4)
Alcohol-related problems**				
No	4,976 (94.2)	620 (94.5)	4,119 (88.9)	541 (88.4)
Yes	308 (5.8)	36 (5.5)	512 (11.1)	71 (11.6)
Previously reported miscarriage††				
No	4,888 (92.5)	563 (85.8)	4,271 (92.2)	522 (85.3)
Yes	315 (6.0)	82 (12.5)	302 (6.5)	78 (12.7)
Previously reported impaired fecundity‡‡				
No	5,045 (95.5)	387 (59.0)	4,380 (94.6)	425 (69.4)
Yes	239 (4.5)	269 (41.0)	251 (5.4)	187 (30.6)

* Self-report of perceived impaired fecundity on the follow-up survey.
† All characteristics assessed from the baseline survey, except for age, which was assessed using the follow-up survey.
‡ Variable measures exposure to pesticides and chemical exposures. The variable was based on self-report of exposure to occupational hazards requiring protective equipment, routine skin contact with paint and/or solvent and/or substances, pesticides applied to the environment, living spaces, and/or to yourself and/or clothing.
§ Self-reported use of medication to treat anxiety, depression, or stress.
‖ Assessed using screening tools for posttraumatic stress disorder, depression, anxiety, or panic.
¶ Self-report of physician diagnosis to any of the following: hypertension, thyroid condition other that cancer, seizures, lupus, diabetes or sugar diabetes, rheumatoid arthritis, and/or frequent bladder infections.
# Heavy weekly drinking is defined as consuming more than seven drinks per week.
** Alcohol-related problems was assessed using the Patient Health Questionnaire.
†† Self-reported miscarriage at baseline is not included in main analyses for the infertility population. Frequencies are given as a part of subanalyses. Number of people missing this variable in Panel 1 = 92, Panel 2 = 70.
‡‡ Self-reported infertility was assessed at baseline.

Table 4
Frequencies, Prevalence, and AOR of Self-Perceived Impaired Fecundity* among Servicewomen in the Millennium Cohort

Models	Panel 1† (n = 5,940)			Panel 2‡ (n = 5,243)		
	N (%)*	AOR	95% CI	N (%)*	AOR	95% CI
Deployment status§						
Nondeployed	485 (10.7)	1.00		418 (11.2)	1.00	
Deployed, without combat	87 (11.0)	0.96	(0.73–1.27)	67 (9.9)	0.86	(0.64–1.15)
Deployed, with combat	84 (13.6)	1.28	(0.95–1.72)	127 (15.1)	1.23	(0.96–1.57)
Cumulative days deployed‖						
0	485 (10.7)	1.00		418 (11.2)	1.00	
1–180	87 (12.2)	1.08	(0.82–1.43)	91 (12.6)	1.10	(0.84–1.42)
>180	84 (12.1)	1.10	(0.83–1.47)	103 (12.9)	1.02	(0.79–1.32)
Life stressors¶						
Low/mild	612 (10.8)	1.00				
Moderate/major	44 (15.5)	1.24	(0.85–1.82)			

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.

* Number and 3-year cumulative prevalence of self-reported perceived impaired fecundity at follow-up.

† Models adjusted for age, race/ethnicity, occupation, pesticide and chemical exposures, heavy drinking, and prior perceived impaired fecundity at baseline.

‡ Models adjust for age, race/ethnicity, occupation, pesticide and chemical exposures, smoking status, psychiatric symptoms, and prior perceived impaired fecundity at baseline.

§ Combat was defined as self-report of having personally experienced at least one of the following combat or combat-like situations: witnessing a person's death due to war, disaster, or tragic event; witnessing instances of physical abuse (torture, beating, rape); dead and/or decomposing bodies; maimed soldiers or civilians; and prisoners of war or refugees. This was assessed on the baseline survey as having occurred during the past 3 years.

‖ Cumulative length deployed was assessed as the total number of days deployed from 3 years before the baseline assessment to the day the baseline survey was completed.

¶ Life stressors was assessed using scoring mechanisms adapted from the Holmes and Rahe Social Readjustment Rating Scale.

(Araneta et al., 2004), our findings are consistent with the few previous studies that found no association between deployment and miscarriages. Although one previous report found an association between duration of deployment and infertility, our study did not find any significant associations between deployment-related factors and infertility (Armed Forces Health Surveillance Center, 2012). Our prospective study, however, was one of the first to be able to incorporate the timing of events and adjust for numerous military, occupational, demographic, and behavioral characteristics that are known to be risk factors for these outcomes. This ability allowed us to account for the potential effects of these characteristics, and to isolate the effects that deployment status and duration of deployment may have on the reproductive health of women Service members. However, we are not suggesting that all types of various deployment exposures, such as burn pits or blast exposures, have no effect on reproductive health. More research is needed to examine if specific deployment experiences may impact reproductive health of servicewomen and women veterans.

A recent study among women who served in Iraq and Afghanistan found an association between mental disorders and adverse reproductive health outcomes (Cohen et al., 2012). This recent study indicates that there may be a possible indirect relationship between combat and negative reproductive health outcomes, owing to combat-related mental disorders. Our study specifically examined deployment experiences after adjusting for several health factors, including mental disorders, and found no association. However, because combat experiences are known to be associated with mental disorders, we performed a subanalysis to investigate if deployment may have an indirect association with these negative reproductive health outcomes. Even after removing some of these potential mediators from our models, only one model indicated a significant association (life stressors with impaired fecundity). The results from these additional analyses further suggest that deployment and combat are neither directly nor indirectly associated with miscarriages or impaired fecundity.

We found prior miscarriage or impaired fecundity was the strongest risk factor associated with subsequent reporting of miscarriage or impaired fecundity at follow-up among both panels. Additionally, a prior history of medical problems (e.g., hypertension, diabetes, hypertension, thyroid conditions) was significantly associated with reporting miscarriage in panel 1. Incremental increase of age, smoking, and heavy alcohol consumption were also found to be significantly correlated with the outcomes. These are known risk factors of adverse reproductive health of women. The fact that our findings are consistent with the previous literature helps validate our study (Armed Forces Health Surveillance Center, 2012; Artini et al., 2013; Bhattacharya, Townend, & Bhattacharya, 2010; Campbell, Lynch, Esterman, & McDermott, 2011; Chiodo et al., 2012).

This study has several limitations. Although we were able to adjust for many known risk factors of adverse reproductive outcomes, other factors known to cause miscarriage or impair fecundity, such as information on the male partner's characteristics and comprehensive female obstetrical/gynecological information, were not available. It is important to consider that women who are pregnant are not allowed to deploy, which may affect the associations between our outcomes and exposures. Our study also lacked precise timing between return from deployment and incidence of miscarriage or onset of impaired fecundity, which was mitigated by the subanalysis performed using medical record data to compare the results obtained from using the self-reported data. The use of medical record data also mitigated the limitation of using a non-standard self-reported measure of impaired fecundity. In addition, self-reported data, including the miscarriage and impaired fecundity data, are subject to recall bias, especially among women who are concerned over the exposures they experienced on their deployment. Self-reported miscarriage data may also be underreported, although many women often do no not visit a health care provider when a miscarriage is experienced or when fertility issues arise, making self-reported data potentially more complete than data from medical records.

This study has several strengths. To our knowledge, this study is one of the first to prospectively analyze the association between military factors and the reproductive outcomes of miscarriage and self-perceived impaired fecundity among women Service members who served in support of the recent conflicts in Iraq and Afghanistan. Further, our sample included all branches of the U.S. military, Reserve and National Guard members, and women from all military occupations. The survey tool also allowed capture of behaviors not found in medical records, such as alcohol consumption and tobacco use, which are known risk factors for these outcomes, as well as military-specific exposures, including combat (Campbell et al., 2011; Chiodo et al., 2012).

Implications for Practice and/or Policy

Our findings of no associations between deployment and these reproductive health outcomes may provide reassurance to women who deploy as well as to DoD and Department of Veterans Affairs leaders and policymakers. Findings associated with adverse reproductive health events in this study were similar to those in the general population. As such, policies and guidelines should continue to focus on the importance of smoking cessation programs, alcohol abuse counseling, and the prevention/treatment of chronic medical conditions.

Conclusions

Women servicemembers who deployed in support of the recent operations in Iraq and Afghanistan did not have an increased odds of miscarriage or perceived impaired fecundity after deployment in our study sample compared with those who had not deployed. Because reproductive health issues include other outcomes in addition to miscarriage and impaired fecundity, and because it was not possible to examine specific environmental exposures associated with deployments or specific combat exposures, additional research on the reproductive health of military personnel is essential to ensure the ongoing health and well-being of our servicemembers and their families.

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14. ABSTRACT

Background: Research on the reproductive health of U.S. servicewomen deployed in support of the recent operations in Iraq and Afghanistan is sparse. The objective of this study was to evaluate whether military experiences, including combat deployment, deployment length, and life stressors during the recent conflicts, were associated with increased odds for miscarriage or impaired fecundity among U.S. servicewomen. Methods: We used data from the Millennium Cohort Study, a large longitudinal military study that began in 2001 and includes military personnel from all service branches, including active duty and Reserve/National Guard personnel. Participants for this study included women aged 18 to 45 years who had completed two questionnaires (2004–2006 and 2007–2008). Separate multivariable logistic regression models were performed to estimate the odds of reporting miscarriage and impaired fecundity by military experiences that adjusted for covariates. Subanalyses were conducted using International Classification of Diseases, Ninth Revision, Clinical Modification codes found in the Military Health System Data Repository for both outcomes among servicewomen on active duty. Results: Overall, 31% and 11% of military servicewomen reported miscarriage and impaired fecundity, respectively, during the approximate 3-year follow-up period. After adjusting for demographic, behavioral, and military characteristics, deployment experiences and life stressors were not associated with miscarriage or perceived impaired fecundity. Subanalyses using medical record data confirmed these results. Conclusions: Overall, these results suggest that military deployments do not increase risk for miscarriage and impaired fecundity among U.S. servicewomen. However, because the point estimates for many of the exposures were elevated, more research is needed to better understand the potential risks associated with environmental exposures and specific types of combat exposures.

15. SUBJECT TERMS

miscarriage, infertility, fecundity, reproductive health, deployment, military, combat, stress

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